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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,499	GUZMAN, NORBERTO A.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *322-429* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *322-429* is/are rejected.

7)☒ Claim(s) *322 and 385* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/25, 3/8/ & 4/29*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments to the specification in the reply filed on April 29, 2006 have been acknowledged and entered.

2. Applicant's amendments to cancel claims 1-321 and add new claims 322-429 in the reply filed on April 29, 2006 have been acknowledged and entered.

3. Claims 322-429 are pending.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on January 25, 2006, March 8, 2006, and April 29, 2006 have been considered by the examiner.

Drawings

5. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: reference numbers 52 (Fig.'s 2, 4, and 6), 26 (Fig. 4), 92 (Fig.'s 7 and 8), 66A (Fig. 14), 37A (Fig. 15), 17A (Fig. 16), 13 (Fig. 18), 170 (Fig. 23B), 140A (Fig. 24A), 150A (Fig. 24A), 160A (Fig. 24A), 170A (Fig. 24B) are not described in the current specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in

compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

6. The drawings are objected to because reference number 46 in Fig. 6 is not referring to the same detector in Fig. 1. It is suggested that applicant change reference number 46 in Fig. 6 to "86." Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either

"Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Objections Withdrawn

7. Applicant's arguments, see p3-31, filed on April 29, 2006, with respect to the objection of the specification have been fully considered and are persuasive. The objection of the specification has been withdrawn in view of the amended specification and canceled claim 36 in the reply filed on April 29, 2006.

8. Applicant's arguments, see p49, filed on April 29, 2006, with respect to the objection of claim 2 have been fully considered and are persuasive. The objection of claim 2 has been withdrawn in view of the canceled claim 2 in the reply filed on April 29, 2006.

Rejections Withdrawn

9. Applicant's arguments, see p49, filed on April 29, 2006, with respect to the rejection under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claims 2, 6, 7, 11, 18, 19, 30, 31, 37, and 38 under 35 U.S.C. 112, second paragraph has been withdrawn in view of the canceled claims 2, 6, 7, 11, 18, 19, 30, 31, 37, and 38 in the reply filed on April 29, 2006.

10. Applicant's arguments, see pp49-54, filed on April 29, 2006, with respect to the following rejections under 35 U.S.C. 103(a) have been fully considered and are persuasive:

- Rejection of claims 1-4, 8-13, 16, 18-23, 29, 31-36, 38, and 39 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. (U.S. Patent No. 6,150,180, Filed June 28, 1996) in view of Lipshutz et al. (U.S. Patent No. 5,856,174, Filed June 29, 1995)
- Rejection of claims 5, 6, 14, 15, 28, and 30 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Nelson et al. (U.S. Patent No. 6,007,690, Filed July 30, 1997)
- Rejection of claims 5, 7, and 30 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 1998, Vol. 715, pp29-54)
- Rejection of claim 17 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Ogan et al. (U.S. Patent No. 4,816,123, Filed Apr. 16, 1986)
- Rejection of claims 24 and 25 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Yeung et al. (U.S. Patent No. 5,324,401, Filed Feb. 5, 1993)

- Rejection of claim 26 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001)
- Rejection of claim 27 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999)
- Rejection of claim 37 under 35 U.S.C. 103(a) as being unpatentable over Parce et al. in view of Lipshutz et al., and further in view of Fuchs et al. (U.S. Patent No. 5,246,577, Filed May 29, 1990)

The rejections of claims 1-39 under 35 U.S.C. 103(a) as listed above have been withdrawn in view of the canceled claims 1-39 in the reply filed on April 29, 2006.

11. Applicant's arguments, see p49, filed on April 29, 2006, with respect to the rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Lipshutz et al. have been fully considered and are persuasive. The rejection of claims 1-9, 12, 13, 16, 20-23, and 33 the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Lipshutz et al. has been withdrawn in view of the canceled claims 1-9, 12, 13, 16, 20-23, and 33 in the reply filed on April 29, 2006.

12. Applicant's arguments, see p49, filed on April 29, 2006, with respect to the provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33 and 34 of copending Application No. 10/821,328 in view of Lipshutz et al. have been fully considered and are persuasive. The provisional rejection of claims 1, 2 and 33 the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33 and 34 of copending Application No. 10/821,328 in view of Lipshutz et al. has been withdrawn in view of the canceled claims 1, 2 and 33 in the reply filed on April 29, 2006.

Specification

13. The use of the trademark SUPERDEX™ (p43, line 19 and p45, paragraph [0163], line 1) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

14. Claim 322 is objected to because of the following informalities: the term "the overlapping portion" in line 11 should be changed to "the passage overlapping portion" to be consistent with the term "a passage overlapping portion" first defined in line 3. Appropriate correction is required.

15. Claim 385 objected to because of the following informalities: the term a comma is needed following the words "concentrator" in lines 3 and 11 and "ligands" in lines 4 and 12. Appropriate correction is required.

Claim Rejections - 35 USC § 112

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 322-429 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

18. Claim 322 recites the limitation "the separation" in line 11. There is insufficient antecedent basis for this limitation in the claim.

19. In claim 322, the term "one sample" in line 14 is vague and indefinite. It is unclear whether or not the term "one sample" in line 14 is referring to "a sample" in line 6. For the purpose of examination, the term "one sample" in line 14 has been interpreted as referring to "a sample" in line 6.

20. Claim 322 recites the limitation "the flow" in lines 14 and 16. There is insufficient antecedent basis for this limitation in the claim.

21. In claims 345, 376, and 405 the phrase " the first and second separation passages flow" is vague and indefinite. How does the first and second separation passages flow? The fluid within the passages can flow but not the separation passages.

22. In claims 345 and 405, the phrase "positioned at a detection zone of the analyte detector system" is vague and indefinite. It is unclear to what term the phrase "positioned at a detection zone of the analyte detector system" is referring. For the purpose of examination, the phrase has been interpreted as referring to the exit outlet.

23. In claims 346, 377, and 407, it is not clear where the "passage bulging members" are located within the passage overlapping region. For the purpose of examination, the claim has been interpreted in light of the specification (Fig.'s 27A and 27B).

24. Claim 347, 378, and 408 recite the limitation "the inner diameter" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

25. In claim 352, the term "first valve means" is vague and indefinite. The term "first valve means" is defined as being associated with the transport passage in claim 322.

The use of the term "first valve means" in claim 352 suggests that the term "first valve means" includes both transport passage and separation passage valves. Therefore, the use of the term "first valve means" in claim 352 is inconsistent with the "first valve means" in claim 322.

26. In claim 353, the term "second valve means" is vague and indefinite. The term "second valve means" is defined as being associated with the separation passage in claim 322. The use of the term "second valve means" in claim 352 suggests that the term "second valve means" includes both transport passage and separation passage valves. Therefore, the use of the term "second valve means" in claim 352 is inconsistent with the "second valve means" in claim 322.

27. In claim 354, the term "a buffer supply" in lines 13 and 23 is vague and indefinite. It is unclear whether or not the term "a buffer supply" in lines 13 and 23 are the same. For the purpose of examination, the terms have been interpreted as being different in light of the current specification (Fig. 1).

28. In claim 385, the phrase "convey by electrophoresis migration" in lines 5 and 13 is vague and indefinite. The specification does not define the phrase and it is not clear what the phrase "convey by electrophoresis migration" means.

29. In claim 385, the phrases "valves operative around the first staggered configuration" and "valves operative around the second staggered configuration" is vague and indefinite. The phrase fails to clearly define the position/location of the valves and therefore fails to define metes and bounds of the valve position/location.

30. In claim 415, the phrase "conveyed by electrophoresis migration" in line 12 is vague and indefinite. The specification does not define the phrase and it is not clear what the phrase "conveyed by electrophoresis migration" means. Furthermore, it is unclear to what term the phrase "conveyed by electrophoresis migration" is referring.

Claim Rejections - 35 USC § 103

31. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

32. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

33. Claims 322, 328-335, 342-345, 347-350, 352, 353, 385, 391-398, 405, 406, 408-411, 413-415, 421-424, 428, and 429 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998).

Frankel et al. teaches an electrophoresis apparatus (Fig. 13) comprising:

- a transport passage (horizontal capillary channel having a port 1303 in Fig. 13) capable of directing flow of a sample solution to be analyzed (column 20, lines 21-35)
- a plurality of separation passages (plurality of vertical capillary channels having microvalves 1310 and 1315) coupled to the transport passage by having a passage overlapping portion overlapping a portion of the transport passage and forming a plurality of analyte concentrators in the passage overlapping portion (1305 in Fig. 13) having immobilized affinity ligands capable of attracting at least one target analyte from the sample solution that passes through each of the analyte concentrators (column 20, lines 21-35); and
- a plurality of valves located on the plurality of separation passages (1310 and 1315 in Fig. 13 and column 20, lines 21-35), wherein the valves control the flow of fluid through each of the plurality of separation passages and conveyed by electrophoresis migration to a detector system

(column 20, lines 36-45) and each of the analyte concentrators are localized by the valves on the separation passages (Fig. 13).

However, Frankel et al. fails to teach an electrophoresis apparatus, further comprising a plurality of valves located on the transport passage, wherein each of the analyte concentrators are localized by the valves on the transport passage and the transport passage entering the separation passage at a side entry location of the analyte concentrator and exiting the separation passage at a side exit location spaced a distance along a length of the separation passage and thereby offset a distance from the separation portion at the entry location, the overlapping portion extending between the entry location and the exit location to form a staggered configuration.

Robotti et al. teaches a microfluidic device comprising two intersecting micro-channels (32 and 34 in Fig.'s 4 and 5) having entry and exit ports and microvalves (36, 38, 39, and 40, positioned along the micro-channels, which localizes the overlapping portion of two intersecting micro-channels, 32 and 34 (Fig.'s 4 and 5 and column 10, lines 13-22). The variation in the placement of micro-channel 34 includes a staggered configuration, wherein the overlapping region of two micro-channels is increased/elongated (Fig. 5). The device of Robotti et al. can be used in a variety of different fluid flow processes such as electrophoretic or chromatographic application (column 10, lines 41-57).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include microvalves positioned along both intersecting transport passage and separation passages as taught by Robotti et al. in the electrophoretic

apparatus of Frankel et al. in order to manipulate fluid flow in applications such as electrophoretic or chromatographic assays, which requires fluid flow control. The advantage of manipulating fluid flow in the transport passage provides the motivation to combine the teachings of Robotti et al. and Frankel et al. with reasonable expectation of success as Robotti et al. teaches that the microvalves positioned along two intersecting channels can be used in applications such as electrophoretic or chromatographic assays. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the overlapping portion (analyte concentrator) of the transport and separation passages of Frankel et al. with the overlapping portion, wherein the overlapping portion extends between the entry location and the exit location of the separation passages to form a staggered configuration as taught by Robotti et al. as both configurations, staggered and non-staggered, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the staggered or non-staggered configuration is used. Furthermore, current specification supports that staggered and non-staggered configurations of the transport passage with respect to the separation passage are art-recognized equivalents in the microfluidic art applications as the originally filed disclosure includes two embodiments of the transport passage and separation passages in staggered and non-staggered configuration, which can function to concentrate an analyte in the analyte concentrators (p22, paragraphs [0106] and [0107]).

With respect to claims 328, 391, and 392, the separation passage of Frankel et al. in view of Robotti et al. is capable of separating the analyte of interest retained by the

immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode of capillary electrophoresis (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "capable of separating the analyte of interest retained by the immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode of capillary electrophoresis" does not structurally limit the separation passage. Therefore, the separation passage of Frankel et al. in view of Robotti et al. meets the currently recited claim as the separation passage would be capable of performing the intended use of separating the analyte of interest retained by the immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode of capillary electrophoresis.

With respect to claims 329, 393, and 421, Frankel et al. teaches an auxiliary passage (1325 in Fig. 13) coupled to at least one of the separation passages downstream of the analyte concentrator to provide a fluid to the separation passage away from the analyte concentrator and valve means (1312 in Fig. 13) for controlling flow out of the auxiliary passage (column 20, lines 21-35).

With respect to claims 330, 394, and 422, Frankel et al. teaches an auxiliary analyte concentrator on one of the separation passages and downstream of the analyte concentrator, the auxiliary analyte concentrator having affinity ligands (1330 in Fig. 13

and column 20, lines 36-45) capable of retaining chromophores to being analyte of interest (fluorescently labeled, column 15, lines 39-53) released from the analyte concentrator (1305 in Fig. 13). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "capable of retaining chromophores to being analyte of interest released from the analyte concentrator to improve sensitivity and selectivity of the analyte of interest." does not structurally limit the auxiliary analyte concentrator having affinity ligands. Therefore, the auxiliary analyte concentrator having affinity ligands of Frankel et al. meets the currently recited claim as the auxiliary analyte concentrator having affinity ligands would be capable of performing the intended use of retaining chromophores to being analyte of interest released from the analyte concentrator to improve sensitivity and selectivity of the analyte of interest.

With respect to claims 331, 332, 395, 396, 423, and 424, Frankel et al. teaches the separation passage filled with a gel matrix and an electrically conductive fluid (column 3, lines 36-53).

With respect to claim 333, Frankel et al. teaches an auxiliary passage (1325 in Fig. 13) through which a separation buffer can be provided to the separation passage and positioned between the analyte concentrator and the detector system (Fig. 13 and column 20, lines 29-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the

prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "through which a separation buffer can be provided to the separation passage" does not structurally limit the auxiliary passage. Therefore, the auxiliary passage of Frankel et al. meets the currently recited claim as the auxiliary passage would be capable of providing a separation buffer to the separation passage.

With respect to claims 334 and 397, Frankel et al. teaches the immobilized affinity ligand, which is capable of performing at least one chemical or biochemical reaction (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "capable of performing at least one chemical or biochemical reaction" does not structurally limit the immobilized affinity ligand. Therefore, the immobilized affinity ligand of Frankel et al. meets the currently recited claim as the immobilized affinity ligand would be capable of performing the intended use of performing at least one chemical or biochemical reaction.

With respect to claims 335 and 398, Frankel et al. teaches the analyte concentrator having a subcellular structure (column 20, lines 21-35), which would be capable of carrying out drug metabolism studies. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention

and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "to carry out drug metabolism studies" does not structurally limit the analyte concentrator having a subcellular structure. Therefore, the analyte concentrator having a subcellular structure of Frankel et al. meets the currently recited claim as the analyte concentrator having a subcellular structure would be capable of carrying out drug metabolism studies.

With respect to claim 343 and 405, Frankel et al. teaches the first and second separation passages merge into a single exit outlet (Fig. 17).

With respect to claims 344 and 345, Frankel et al. teaches the second valve means (1315 in Fig. 13) controls the sequential fluid flow from the first and second separation passages to the exit outlet passage at the merging of the separation passages into the exit outlet passage (1325 in Fig. 13).

With respect to claims 347 and 408, Frankel et al. in view of Robotti et al. discloses the claimed invention except for the inner diameter of the transport passage is larger than the inner diameter of the separation passage. It would have been obvious to one having ordinary skill in the art at the time of the invention to adjust the diameter of the transport and separation passage to have the inner diameter of the transport passage is larger than the inner diameter of the separation passage in order to optimize the fluid flow rate within the transport and separation passages during affinity-based CE assays, since it has been held that where the general conditions of a claim are

disclosed in the prior art, discovering the optimum or workable range involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

With respect to claims 348 and 409, Robotti et al. teaches the first and second valve means on the transport and separation passages, respectively, on both sides of the analyte concentrator in order to manipulate fluid flow along the transport and separation passages (Fig. 5).

With respect to claim 349, 410, and 428, Frankel et al. teaches the transport and the separation passages are both capillaries (column 20, lines 46-57).

With respect to claim 350, 411, and 429, Frankel et al. teaches the transport and the separation passages are both channels (column 19, lines 54-55).

With respect to claims 352, 353, 406, 413, and 414, Robotti et al. teaches the first valve and second valve means, which includes transport passage valves, which are adapted to be opened or closed to allow the sample to pass through the analyte concentrator (column 20, lines 21-35), and the separation passage valves, which are adapted to be opened or closed to allow buffer solution to pass through the analyte concentrator towards the detector system (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "adapted to be opened or closed to allow the sample to pass through the analyte concentrator" and "adapted to be opened or closed to allow buffer solution to

pass through the analyte concentrator towards the detector system" does not structurally limit the first valve and second valve means. Therefore, the first valve and second valve means of Frankel et al. meets the currently recited claim as the first valve and second valve means would be capable of being adapted to be opened or closed to allow the sample to pass through the analyte concentrator and adapted to be opened or closed to allow buffer solution to pass through the analyte concentrator towards the detector system.

34. Claims 323-327, 338-341, 351, 386-390, 401-404, 412, 416-420, and 425-427 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322, 354, 385, and 415 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54).

Frankel et al. in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. fails to teach an electrophoresis apparatus, wherein the analyte concentrator includes a matrix assembly having a surface to which the immobilized affinity ligand is bound.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis (CE, p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). Often, high analyte concentrators are required to have sufficient material for detection in the

capillary (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). In this regard, a series of solid-phase microextraction devices, termed 'analyte concentrators' have been developed for selective and/or non-selective preconcentration on-line with CE (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). One of the analyte concentrator designs include beads, to which an affinity compound is attached, embraced between two frits (pressure-resistant porous end walls) forming a microaffinity column (a matrix assembly) located within a separation capillary passage (Fig. 17 and p47, right column). The enrichment chamber design permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability (p47, right column).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of Frankel et al. in view of Robotti et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of Heegaard et al. and Frankel et al. in view of Robotti et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE.

With respect to claims 324, 326, 387, 389, 417, and 419, Heegaard et al. teaches the matrix assembly including a fixed architecture defined by beaded microstructures interconnected to each other and to the passage overlapping portion (beads, p47, right column) as the current specification (p19, paragraph [0101]) defines interconnected beads as being as beads coated with binding members (affinity ligands) such as lectin, enzyme, cofactor, Protein A, antibody, antigen, and oligonucleotide (column 5, lines 50-65).

With respect to claims 325, 388, and 418, Heegaard et al. teaches the analyte concentrator, which retains the matrix assembly by pressure-resistant porous end walls (frits) disposed in the separation passage (Fig. 17 and p47, right column). The pressure-resistant porous end walls are place in the inlet and outlet of the analyte concentrator (Fig. 17). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include pressure-resistant porous end walls (frits) disposed in the inlets and outlets of the analyte concentrator in the separation passage and transport passage in order to embrace (retain) the matrix assembly within the overlapping portion of the analyte concentrator.

With respect to claims 327, 390, and 420, Heegaard et al. teaches an analyte concentrator, where the matrix assembly includes a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion (Fig. 10).

With respect to claims 338, 351, 401, and 412, Heegaard et al. teaches the matrix assembly with covalently bound affinity ligand (p47, right column).

With respect to claims 339-341, 402-404, and 425-427 Heegaard et al. teaches the use of variety of detection systems including ultraviolet, laser-induced fluorescence, and mass spectrometer detector systems in order to detect affinity interactions using CE having an analyte concentrator (p43, left column, second paragraph).

35. Claims 336 and 399 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322 and 385 above, and further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001).

Frankel et al. in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. fails to teach an electrophoretic apparatus, wherein each of the analyte concentrators has an acoustic micromixing system to improve the reaction in the analyte concentrators.

Yamanishi et al. teaches filtration chamber comprising acoustic elements to apply physical forces to promote, enhance, or facilitate processing or desired biochemical reactions of a sample (pp14-15, paragraph [0169]). For example, acoustic elements can cause mixing of the components within the chamber, thereby dislodging nonfilterable components from the slots or pores (p14, paragraph [0169], lines 16-19).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of Frankel et al. in view of Robotti et al. with acoustic micromixing system of Yamanishi et al. in order to promote, enhance, or

facilitate processing or desired biochemical reactions of a sample by mixing of the components within the analyte concentrators of Frankel et al. in view of Robotti et al. The advantage of promoting, enhancing or facilitating desired biochemical reactions of a sample by mixing of the components within the analyte concentrators provides the motivation to combine the teachings of Yamanishi et al. and Frankel et al. in view of Robotti et al. with a reasonable expectation of success as the acoustic micromixing system of Yamanishi et al. is used to cause mixing in biochemical reactions.

36. Claims 337 and 400 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322 and 385 above, and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999).

Frankel et al. in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. fails to teach an electrophoretic apparatus, where each of the analyte concentrators has a microwave pulse system to improve the reaction in the analyte concentrators.

Barenburg et al. teaches a microwave radiation device, which is applied to chemical reactions and processes, including nucleic acid extraction from microorganisms, enhances, or sometimes make possible the desired result (p2, paragraph [0010]). Thus, there is a need in the art for microfluidic devices in which

microwave radiation can be applied to the reaction cavities within the device (p2, paragraph [0010]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of Frankel et al. in view of Robotti et al. with a microwave pulse system for applying microwave radiation to a cavity within a microfluidic device as taught by Barenburg et al. in order to enhance or sometimes make possible the desired result of chemical reactions and processes (improve the reaction in the analyte concentrators). The advantage of enhancing or make possible the desired result of chemical reactions and processes within the analyte concentrators provides the motivation to combine the teachings of Barenburg et al. and Frankel et al. in view of Robotti et al. with a reasonable expectation of success as Barenburg et al. teaches that a microwave pulse system can be used to enhance or sometimes make possible the desired result of chemical reactions.

37. Claims 346 and 407 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322 and 385 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54) and Fuchs et al. (U.S. Patent No. 5,246,577, Filed May 29, 1990).

Frankel et al. in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. fails to teach an

electrophoretic apparatus, where the concentration area is surrounded by bulging members to retain the matrix containing immobilized affinity ligands within the concentration area.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis (CE, p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). Often, high analyte concentrators are required to have sufficient material for detection in the capillary (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). In this regard, a series of solid-phase microextraction devices, termed 'analyte concentrators' have been developed for selective and/or non-selective preconcentration on-line with CE (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). One of the analyte concentrator designs include beads, to which an affinity compound is attached, embraced between two frits (pressure-resistant porous end walls) forming a microaffinity column (a matrix assembly) located within a separation capillary passage (Fig. 17 and p47, right column). The enrichment chamber design permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability (p47, right column).

Fuchs et al. teaches an apparatus for concentrating a solute sample, which can be subsequently released for analysis by capillary electrophoresis (CE, Abstract). The apparatus comprises a capillary tube containing a short length of packed particles or gel adapted to retain sample solutes, which particles are retained in the capillary tube by

constrictions (concentration area surrounded by bulging members, Abstract and Fig. 1). The apparatus of Fuchs et al. permits the use of CE to analyze samples having low concentration of analytes (column 1, lines 3-31).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of Frankel et al. in view of Robotti et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of Heegaard et al. and Frankel et al. in view of Robotti et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ inlet and outlet of the overlapping portion surrounded by bulging members as taught by Fuchs et al. in the analyte concentrator of Heegaard et al. in order to confine (retain) the matrix containing immobilized affinity ligands (column 1, lines 21-25) within the concentration area since both configurations, the overlapping portion surrounded by bulging members or frits, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the overlapping portion surrounded by bulging members or frits is used to retain the matrix assembly within the overlapping portion of the analyte concentrator. Furthermore, current specification

supports that different embodiments for analyte concentrators with or without frit (p25, paragraph [0112]) are art-recognized equivalents as the originally filed disclosure includes several embodiments, which include the analyte concentrators with frit or bulging members surrounding the overlapping portion. Both embodiments can function to retain matrix assembly in the overlapping portion of the analyte concentrators (p22, paragraphs [0106] and [0107]).

38. Claims 354, 361-367, 374-376, 378-381, 383, and 384 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996).

Frankel et al. teaches an electrophoresis apparatus (Fig. 13) comprising:

- a transport passage (horizontal capillary channel having a port 1303 in Fig. 13) capable of directing flow of a sample solution to be analyzed (column 20, lines 21-35)
- a plurality of separation passages (plurality of vertical capillary channels having microvalves 1310 and 1315) coupled to the transport passage by having a passage overlapping portion overlapping a portion of the transport passage and forming a plurality of analyte concentrators in the passage overlapping portion (1305 in Fig. 13) having immobilized affinity ligands capable of attracting at least one target analyte from the sample

solution that passes through each of the analyte concentrators (column 20, lines 21-35); and

- a plurality of valves (valve system) located on the plurality of separation passages (1310 and 1315 in Fig. 13 and column 20, lines 21-35), wherein the valves control the flow of fluid through each of the plurality of separation passages and conveyed by electrophoresis migration to a detector system (column 20, lines 36-45) and each of the analyte concentrators are localized by the valves on the separation passages (Fig. 13).

Frankel et al. further teaches one buffer supply (1302 in Fig. 13) associated with the first and second separation passages. However, Frank et al. fails to teach that each of the first and second separation passages are associated with first and second buffer supplies. Frankel et al. further fails to teach an electrophoresis apparatus, further comprising a plurality of valves located on the transport passage, wherein each of the analyte concentrators are localized by the valves on the transport passage and the transport passage entering the separation passage at a side entry location of the analyte concentrator and exiting the separation passage at a side exit location spaced a distance along a length of the separation passage and thereby offset a distance from the separation portion at the entry location, the overlapping portion extending between the entry location and the exit location to form a staggered configuration.

Robotti et al. teaches a microfluidic device comprising two intersecting micro-channels (32 and 34 in Fig.'s 4 and 5) having entry and exit ports and microvalves (36,

38, 39, and 40, positioned along the micro-channels, which localizes the overlapping portion of two intersecting micro-channels, 32 and 34 (Fig.'s 4 and 5 and column 10, lines 13-22). The variation in the placement of micro-channel 34 includes a staggered configuration, wherein the overlapping region of two micro-channels is increased/elongated (Fig. 5). The device of Robotti et al. can be used in a variety of different fluid flow processes such as electrophoretic or chromatographic application (column 10, lines 41-57).

Yeung et al. teaches a capillary electrophoresis system containing an array of capillaries (column 7, lines 20-33), wherein either a common buffer container or separate buffer vials are in fluid communication with the individual capillaries (column 7, lines 46-49).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include microvalves positioned along both intersecting transport passage and separation passages as taught by Robotti et al. in the electrophoretic apparatus of Frankel et al. in order to manipulate fluid flow in applications such as electrophoretic or chromatographic assays, which requires fluid flow control. The advantage of manipulating fluid flow in the transport passage provides the motivation to combine the teachings of Robotti et al. and Frankel et al. with reasonable expectation of success as Robotti et al. teaches that the microvalves positioned along two intersecting channels can be used in applications such as electrophoretic or chromatographic assays. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the overlapping portion (analyte concentrator) of the

transport and separation passages of Frankel et al. with the overlapping portion, wherein the overlapping portion extends between the entry location and the exit location of the separation passages to form a staggered configuration as taught by Robotti et al. as both configurations, staggered and non-staggered, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the staggered or non-staggered configuration is used. Furthermore, current specification supports that staggered and non-staggered configurations of the transport passage with respect to the separation passage are art-recognized equivalents in the microfluidic art applications as the originally filed disclosure includes two embodiments of the transport passage and separation passages in staggered and non-staggered configuration, which can function to concentrate an analyte in the analyte concentrators (p22, paragraphs [0106] and [0107]). Moreover, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a common buffer supply of Frankel et al. with a buffer supply system, wherein each capillary is in fluid communication with separate buffer vials, as taught by Yeung et al. since the two buffer supply systems are art-recognized equivalents in the electrophoresis applications, where it is immaterial whether the one common buffer supply or separate buffer supply in fluid communication with individual capillary is used to supply buffer to the separation passage of the electrophoresis apparatus.

With respect to claim 361, the separation passage of Frankel et al. in view of Robotti et al. is capable of separating the analyte of interest retained by the immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode

of capillary electrophoresis (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "capable of separating the analyte of interest retained by the immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode of capillary electrophoresis" does not structurally limit the separation passage. Therefore, the separation passage of Frankel et al. in view of Robotti et al. meets the currently recited claim as the separation passage would be capable of performing the intended use of separating the analyte of interest retained by the immobilized affinity ligand after the analyte is released from the affinity ligand by at least one mode of capillary electrophoresis.

With respect to claim 362, Frankel et al. teaches an auxiliary passage (1325 in Fig. 13) coupled to at least one of the separation passages downstream of the analyte concentrator to provide a fluid to the separation passage away from the analyte concentrator and valve means (1312 in Fig. 13) for controlling flow out of the auxiliary passage (column 20, lines 21-35).

With respect to claim 363, Frankel et al. teaches an auxiliary analyte concentrator on one of the separation passages and downstream of the analyte concentrator, the auxiliary analyte concentrator having affinity ligands (1330 in Fig. 13 and column 20, lines 36-45) capable of retaining chromophores to being analyte of

interest (fluorescently labeled, column 15, lines 39-53) released from the analyte concentrator (1305 in Fig. 13). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "capable of retaining chromophores to being analyte of interest released from the analyte concentrator to improve sensitivity and selectivity of the analyte of interest." does not structurally limit the auxiliary analyte concentrator having affinity ligands. Therefore, the auxiliary analyte concentrator having affinity ligands of Frankel et al. meets the currently recited claim as the auxiliary analyte concentrator having affinity ligands would be capable of performing the intended use of retaining chromophores to being analyte of interest released from the analyte concentrator to improve sensitivity and selectivity of the analyte of interest.

With respect to claims 364 and 365, Frankel et al. teaches the separation passage filled with a gel matrix and an electrically conductive fluid (column 3, lines 36-53).

With respect to claim 366, Frankel et al. teaches the immobilized affinity ligand, which is capable of performing at least one chemical or biochemical reaction (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The

intended use of the claimed invention, "capable of performing at least one chemical or biochemical reaction" does not structurally limit the immobilized affinity ligand. Therefore, the immobilized affinity ligand of Frankel et al. meets the currently recited claim as the immobilized affinity ligand would be capable of performing the intended use of performing at least one chemical or biochemical reaction.

With respect to claim 367, Frankel et al. teaches the analyte concentrator having a subcellular structure (column 20, lines 21-35), which would be capable of carrying out drug metabolism studies. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "to carry out drug metabolism studies" does not structurally limit the analyte concentrator having a subcellular structure. Therefore, the analyte concentrator having a subcellular structure of Frankel et al. meets the currently recited claim as the analyte concentrator having a subcellular structure would be capable of carrying out drug metabolism studies.

With respect to claims 374-376, Frankel et al. in view of Robotti et al. and Yeung et al. teaches the first and second separation passages merge into a single exit outlet, wherein the valve system controls the sequential fluid flow of the first and second separation passages to the detection zone (Fig. 13). A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from

the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "wherein the valve system controls the sequential fluid flow of the first and second separation passages to the detection zone" does not structurally limit the valve system. Therefore, the valve system structure of Frankel et al. in view of Robotti et al. and Yeung et al. meets the currently recited claim as the valve system would be capable of controlling the sequential fluid flow of the first and second separation passages to the detection zone.

With respect to claim 375, Robotti et al. teaches the first and second valve means on the transport and separation passages, respectively, on both sides of the analyte concentrator in order to manipulate fluid flow along the transport and separation passages (Fig. 5).

With respect to claim 378, Frankel et al. in view of Robotti et al. and Yeung et al. discloses the claimed invention except for the inner diameter of the transport passage is larger than the inner diameter of the separation passage. It would have been obvious to one having ordinary skill in the art at the time of the invention to adjust the diameter of the transport and separation passage to have the inner diameter of the transport passage is larger than the inner diameter of the separation passage in order to optimize the fluid flow rate within the transport and separation passages during affinity-based CE assays, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable range involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

With respect to claim 380, Frankel et al. teaches the transport and the separation passages are both capillaries (column 20, lines 46-57).

With respect to claim 381, Frankel et al. teaches the transport and the separation passages are both channels (column 19, lines 54-55).

With respect to claims 383 and 384, Robotti et al. teaches the valve system, which includes transport passage valves, which are adapted to be opened or closed to allow the sample to pass through the analyte concentrator (column 20, lines 21-35), and the separation passage valves, which are adapted to be opened or closed to allow buffer solution to pass through the analyte concentrator towards the detector system (column 20, lines 21-35). Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The intended use of the claimed invention, "adapted to be opened or closed to allow the sample to pass through the analyte concentrator" and "adapted to be opened or closed to allow buffer solution to pass through the analyte concentrator towards the detector system" does not structurally limit the first valve and second valve means. Therefore, the first valve and second valve means of Frankel et al. meets the currently recited claim as the first valve and second valve means would be capable of being adapted to be opened or closed to allow the sample to pass through the analyte concentrator and adapted to be opened or closed to allow buffer solution to pass through the analyte concentrator towards the detector system.

39. Claims 355-360, 370-373, and 382 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54).

Frankel et al. in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. and Yeung et al. fails to teach an electrophoresis apparatus, wherein the buffer supply of the first separation passage includes a separation buffer to release the bound first analyte of interest from the immobilized affinity ligands of the first analyte concentrator and the analyte concentrator includes a matrix assembly having a surface to which the immobilized affinity ligand is bound.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis (CE, p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). Often, high analyte concentrators are required to have sufficient material for detection in the capillary (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). In this regard, a series of solid-phase microextraction devices, termed 'analyte concentrators' have been developed for selective and/or non-selective preconcentration on-line with CE (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary*

electrophoresis). One of the analyte concentrator designs include beads, to which an affinity compound is attached, embraced between two frits (pressure-resistant porous end walls) forming a microaffinity column (a matrix assembly) located within a separation capillary passage (Fig. 17 and p47, right column). The enrichment chamber design permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability (p47, right column). Following the capturing of sample components (analytes of interest), a small volume of eluting solution is passed through the analyte concentrator to remove the absorbed sample components, which in smaller volume for the separation by capillary electrophoresis of the concentrated target analyte, which requires electrophoresis separation buffer (pp42-43, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*, first paragraph and p36, right column, second paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to further include elution buffer and separation buffer of Heegaard et al. in the buffer supply system of Frankel et al. in view of Robotti et al. and Yeung et al. in order to perform affinity based CE separations. The advantage of having necessary buffers to conduct affinity-base CE separation, which allows concentration of target analytes prior to CE separation for increased sensitivity, provides the motivation to combine the teachings of Heegaard et al. and Frankel et al. in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the apparatus of Frankel et al. is designed for affinity-based CE separation. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix

assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of Frankel et al. in view of Robotti et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of Heegaard et al. and Frankel et al. in view of Robotti et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE.

With respect to claims 357 and 359, Heegaard et al. teaches the matrix assembly including a fixed architecture defined by beaded microstructures interconnected to each other and to the passage overlapping portion (beads, p47, right column) as the current specification (p19, paragraph [0101]) defines interconnected beads as being as beads coated with binding members (affinity ligands) such as lectin, enzyme, cofactor, Protein A, antibody, antigen, and oligonucleotide (column 5, lines 50-65).

With respect to claim 358, Heegaard et al. teaches the analyte concentrator, which retains the matrix assembly by pressure-resistant porous end walls (frits) disposed in the separation passage (Fig. 17 and p47, right column). The pressure-resistant porous end walls are place in the inlet and outlet of the analyte concentrator (Fig. 17). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include pressure-resistant porous end walls (frits) disposed in the inlets and outlets of the analyte concentrator in the separation passage and

transport passage in order to embrace (retain) the matrix assembly within the overlapping portion of the analyte concentrator.

With respect to claim 360, Heegaard et al. teaches an analyte concentrator, where the matrix assembly includes a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion (Fig. 10).

With respect to claims 370 and 382, Heegaard et al. teaches the matrix assembly with covalently bound affinity ligand (p47, right column).

With respect to claims 371-373, Heegaard et al. teaches the use of variety of detection systems including ultraviolet, laser-induced fluorescence, and mass spectrometer detector systems in order to detect affinity interactions using CE having an analyte concentrator (p43, left column, second paragraph).

40. Claim 368 is rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001).

Frankel et al. in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, wherein each of the analyte

concentrators has an acoustic micromixing system to improve the reaction in the analyte concentrators.

Yamanishi et al. teaches filtration chamber comprising acoustic elements to apply physical forces to promote, enhance, or facilitate processing or desired biochemical reactions of a sample (pp14-15, paragraph [0169]). For example, acoustic elements can cause mixing of the components within the chamber, thereby dislodging nonfilterable components from the slots or pores (p14, paragraph [0169], lines 16-19).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of Frankel et al. in view of Robotti et al. and Yeung et al. with acoustic micromixing system of Yamanishi et al. in order to promote, enhance, or facilitate processing or desired biochemical reactions of a sample by mixing of the components within the analyte concentrators of Frankel et al. in view of Robotti et al. and Yeung et al. The advantage of promoting, enhancing or facilitating desired biochemical reactions of a sample by mixing of the components within the analyte concentrators provides the motivation to combine the teachings of Yamanishi et al. and Frankel et al. in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the acoustic micromixing system of Yamanishi et al. is used to cause mixing in biochemical reactions.

41. Claim 369 is rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec.

10, 1996) as applied to claim 354 above, and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999).

Frankel et al. in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, where each of the analyte concentrators has a microwave pulse system to improve the reaction in the analyte concentrators.

Barenburg et al. teaches a microwave radiation device, which is applied to chemical reactions and processes, including nucleic acid extraction from microorganisms, enhances, or sometimes make possible the desired result (p2, paragraph [0010]). Thus, there is a need in the art for microfluidic devices in which microwave radiation can be applied to the reaction cavities within the device (p2, paragraph [0010]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of Frankel et al. in view of Robotti et al. and Yeung et al. with a microwave pulse system for applying microwave radiation to a cavity within a microfluidic device as taught by Barenburg et al. in order to enhance or sometimes make possible the desired result of chemical reactions and processes (improve the reaction in the analyte concentrators). The advantage of enhancing or make possible the desired result of chemical reactions and processes within the analyte concentrators provides the motivation to combine the teachings of Barenburg et al. and Frankel et al. in view of Robotti et al. and Yeung et al. with a reasonable expectation of

success as Barenburg et al. teaches that a microwave pulse system can be used to enhance or sometimes make possible the desired result of chemical reactions.

42. Claim 377 is rejected under 35 U.S.C. 103(a) as being unpatentable over Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997) in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54) and Fuchs et al. (U.S. Patent No. 5,246,577, Filed May 29, 1990).

Frankel et al. in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, Frankel et al. in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, where the concentration area is surrounded by bulging members to retain the matrix containing immobilized affinity ligands within the concentration area.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis (CE, p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). Often, high analyte concentrators are required to have sufficient material for detection in the capillary (p42, right column, *4.1. On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis*). In this regard, a series of solid-phase microextraction devices, termed 'analyte concentrators' have been developed for selective and/or non-selective preconcentration on-line with CE (p42, right column, *4.1.*

On-line solid-phase extraction or preconcentration chambers for capillary electrophoresis). One of the analyte concentrator designs include beads, to which an affinity compound is attached, embraced between two frits (pressure-resistant porous end walls) forming a microaffinity column (a matrix assembly) located within a separation capillary passage (Fig. 17 and p47, right column). The enrichment chamber design permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability (p47, right column).

Fuchs et al. teaches an apparatus for concentrating a solute sample, which can be subsequently released for analysis by capillary electrophoresis (CE, Abstract). The apparatus comprises a capillary tube containing a short length of packed particles or gel adapted to retain sample solutes, which particles are retained in the capillary tube by constrictions (concentration area surrounded by bulging members, Abstract and Fig. 1). The apparatus of Fuchs et al. permits the use of CE to analyze samples having low concentration of analytes (column 1, lines 3-31).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of Frankel et al. in view of Robotti et al. and Yeung et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of

Heegaard et al. and Frankel et al. in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ inlet and outlet of the overlapping portion surrounded by bulging members as taught by Fuchs et al. in the analyte concentrator of Heegaard et al. in order to confine (retain) the matrix containing immobilized affinity ligands (column 1, lines 21-25) within the concentration area since both configurations, the overlapping portion surrounded by bulging members or frits, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the overlapping portion surrounded by bulging members or frits is used to retain the matrix assembly within the overlapping portion of the analyte concentrator. Furthermore, current specification supports that different embodiments for analyte concentrators with or without frit (p25, paragraph [0112]) are art-recognized equivalents as the originally filed disclosure includes several embodiments, which include the analyte concentrators with frit or bulging members surrounding the overlapping portion. Both embodiments can function to retain matrix assembly in the overlapping portion of the analyte concentrators (p22, paragraphs [0106] and [0107]).

Double Patenting

43. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

44. U.S. Patent No. 6,406,604

Claims 322-326, 328, 330, 334, 335, 342, 347, 349-350, 352, 353, 385-389, 391, 392, 394, 397, 398, 406, 408-411, 413-419, 422, 428, and 429 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998).

U.S. Patent No. 6,406,604 teaches an electrophoresis apparatus comprising a transport capillary capable of directing flow of a sample solution to be analyzed, a plurality of separation capillaries coupled to the transport capillary forming a plurality of analyte concentrators having affinity ligands capable of attracting at least one analyte of interest from the sample solution that passes through each of the analyte concentrators. However, U.S. Patent No. 6,406,604 fails to specifically teach a plurality of valves located on the transport capillary and on the plurality of separation capillaries, where the valves on the transport capillary control the flow of the sample solution through the transport capillary and the valves on the plurality of separation capillaries control the flow of fluid through each of the plurality of separation capillaries, whereby each of the

analyte concentrators can be localized by the valves on the transport and the plurality of separation capillaries and the transport passage entering the separation passage at a side entry location of the analyte concentrator and exiting the separation passage at a side exit location spaced a distance along a length of the separation passage and thereby offset a distance from the separation portion at the entry location, the overlapping portion extending between the entry location and the exit location to form a staggered configuration.

Robotti et al. teaches a microfluidic device as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include microvalves positioned along both intersecting transport passage and separation passages as taught by Robotti et al. in the electrophoretic apparatus of U.S. Patent No. 6,406,604 in order to manipulate fluid flow in applications such as electrophoretic or chromatographic assays, which requires fluid flow control. The advantage of manipulating fluid flow in the transport passage provides the motivation to combine the teachings of Robotti et al. and U.S. Patent No. 6,406,604 with reasonable expectation of success as Robotti et al. teaches that the microvalves positioned along two intersecting channels can be used in applications such as electrophoretic or chromatographic assays. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the overlapping portion (analyte concentrator) of the transport and separation passages of U.S. Patent No. 6,406,604 with the overlapping portion, wherein the overlapping portion extends between the entry location and the exit location of the separation passages to form a

staggered configuration as taught by Robotti et al. as both configurations, staggered and non-staggered, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the staggered or non-staggered configuration is used. Furthermore, current specification supports that staggered and non-staggered configurations of the transport passage with respect to the separation passage are art-recognized equivalents in the microfluidic art applications as the originally filed disclosure includes two embodiments of the transport passage and separation passages in staggered and non-staggered configuration, which can function to concentrate an analyte in the analyte concentrators (p22, paragraphs [0106] and [0107]).

Claims 327, 338-341, 351, 390, 401-404, 412, 416-420, and 425-427 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 323, 385, and 415 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54).

U.S. Patent No. 6,406,604 in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. fails to teach an electrophoresis apparatus, wherein the matrix assembly includes a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis as discussed above. One of the analyte concentrator designs include beads, to which an affinity compound is attached, embraced between two frits (pressure-resistant porous end walls) forming a microaffinity column (a matrix assembly) located within a separation capillary passage (Fig. 17 and p47, right column) and a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the separation passage (Fig. 10).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute beaded microstructure of the analyte concentrator of U.S. Patent No. 6,406,604 in view of Robotti et al. with a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion as taught by Heegaard et al. as both configurations, beaded microstructure and a fixed architecture that is fabricated from polymeric microstructures, are art-recognized equivalents in the pre-concentrator applications, where it is immaterial whether the beaded microstructure or the fixed architecture that is fabricated from polymeric microstructures is used.

Claims 329, 331, 332, 343-345, 393, 395, 405, 423, and 424 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 323, 385, and

415 above, and further in view of Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997).

U.S. Patent No. 6,406,604 in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. fails to teach an electrophoresis apparatus, further comprising an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means for controlling fluid flow out of auxiliary passage.

Frankel et al. teaches an electrophoresis apparatus as discussed above. Specifically, Frankel et al. teaches an auxiliary passage (1325 in Fig. 13) coupled to at least one of the separation passages downstream of the analyte concentrator to provide a fluid to the separation passage away from the analyte concentrator and valve means (1312 in Fig. 13) for controlling flow out of the auxiliary passage (column 20, lines 21-35).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means as taught by Frankel et al. in the electrophoretic apparatus of U.S. Patent No. 6,406,604 in view of Robotti et al. in order to manipulate fluid movement from the analyte concentrator down the separation passage to the detector system for CE analysis of eluted analytes.

Claims 336 and 399 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S.

Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 323 and 385 above, and further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001).

U.S. Patent No. 6,406,604 in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. fails to teach an electrophoretic apparatus, wherein each of the analyte concentrators has an acoustic micromixing system to improve the reaction in the analyte concentrators.

Yamanishi et al. teaches a filtration chamber comprising acoustic elements as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of U.S. Patent No. 6,406,604 in view of Robotti et al. with acoustic micromixing system of Yamanishi et al. in order to promote, enhance, or facilitate processing or desired biochemical reactions of a sample by mixing of the components within the analyte concentrators of U.S. Patent No. 6,406,604 in view of Robotti et al. The advantage of promoting, enhancing or facilitating desired biochemical reactions of a sample by mixing of the components within the analyte concentrators provides the motivation to combine the teachings of Yamanishi et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. with a reasonable expectation of success as the acoustic micromixing system of Yamanishi et al. is used to cause mixing in biochemical reactions.

Claims 337 and 400 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 323 and 385 above, and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999).

U.S. Patent No. 6,406,604 in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. fails to teach an electrophoretic apparatus, where each of the analyte concentrators has a microwave pulse system to improve the reaction in the analyte concentrators.

Barenburg et al. teaches a microwave radiation device as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of U.S. Patent No. 6,406,604 in view of Robotti et al. with a microwave pulse system for applying microwave radiation to a cavity within a microfluidic device as taught by Barenburg et al. in order to enhance or sometimes make possible the desired result of chemical reactions and processes (improve the reaction in the analyte concentrators). The advantage of enhancing or make possible the desired result of chemical reactions and processes within the analyte concentrators provides the motivation to combine the teachings of Barenburg et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. with a reasonable expectation of success as Barenburg et al. teaches that a microwave pulse system can be used to enhance or sometimes make possible the desired result of chemical reactions.

Claims 346 and 407 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 323 and 385 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54) and Fuchs et al. (U.S. Patent No. 5,246,577, Filed May 29, 1990).

U.S. Patent No. 6,406,604 t in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. fails to teach an electrophoretic apparatus, wherein the concentration area is surrounded by bulging members to retain the matrix containing immobilized affinity ligands within the concentration area.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis as discussed above.

Fuchs et al. teaches an apparatus for concentrating a solute sample as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of U.S. Patent No. 6,406,604 in view of Robotti et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte

concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of Heegaard et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ inlet and outlet of the overlapping portion surrounded by bulging members as taught by Fuchs et al. in the analyte concentrator of Heegaard et al. in order to confine (retain) the matrix containing immobilized affinity ligands (column 1, lines 21-25) within the concentration area since both configurations, the overlapping portion surrounded by bulging members or frits, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the overlapping portion surrounded by bulging members or frits is used to retain the matrix assembly within the overlapping portion of the analyte concentrator. Furthermore, current specification supports that different embodiments for analyte concentrators with or without frit (p25, paragraph [0112]) are art-recognized equivalents as the originally filed disclosure includes several embodiments, which include the analyte concentrators with frit or bulging members surrounding the overlapping portion. Both embodiments can function to retain matrix assembly in the overlapping portion of the analyte concentrators (p22, paragraphs [0106] and [0107]).

Claims 354, 356-359, 361, 363, 366, 367, 378-381, 383, and 384 are rejected under the judicially created doctrine of obviousness-type double patenting as being

unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998), and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996).

U.S. Patent No. 6,406,604 teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 fails to specifically teach a plurality of valves located on the transport capillary and on the plurality of separation capillaries, where the valves on the transport capillary control the flow of the sample solution through the transport capillary and the valves on the plurality of separation capillaries control the flow of fluid through each of the plurality of separation capillaries, whereby each of the analyte concentrators can be localized by the valves on the transport and the plurality of separation capillaries and the transport passage entering the separation passage at a side entry location of the analyte concentrator and exiting the separation passage at a side exit location spaced a distance along a length of the separation passage and thereby offset a distance from the separation portion at the entry location, the overlapping portion extending between the entry location and the exit location to form a staggered configuration. U.S. Patent No. 6,406,604 further fails to teach an electrophoretic apparatus, wherein each of the first and second separation passages are associated with first and second buffer supplies.

Robotti et al. teaches a microfluidic device comprising two intersecting micro-channels as discussed above.

Yeung et al. teaches a capillary electrophoresis system containing an array of capillaries as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include microvalves positioned along both intersecting transport passage and separation passages as taught by Robotti et al. in the electrophoretic apparatus of U.S. Patent No. 6,406,604 in order to manipulate fluid flow in applications such as electrophoretic or chromatographic assays, which requires fluid flow control. The advantage of manipulating fluid flow in the transport passage provides the motivation to combine the teachings of Robotti et al. and U.S. Patent No. 6,406,604 with reasonable expectation of success as Robotti et al. teaches that the microvalves positioned along two intersecting channels can be used in applications such as electrophoretic or chromatographic assays. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the overlapping portion (analyte concentrator) of the transport and separation passages of U.S. Patent No. 6,406,604 with the overlapping portion, wherein the overlapping portion extends between the entry location and the exit location of the separation passages to form a staggered configuration as taught by Robotti et al. as both configurations, staggered and non-staggered, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the staggered or non-staggered configuration is used. Furthermore, current specification supports that staggered and non-staggered configurations of the transport passage with respect to the separation passage are art-recognized equivalents in the microfluidic art applications as the originally filed disclosure includes two embodiments of the transport passage and separation passages in staggered and non-staggered configuration, which can function to

concentrate an analyte in the analyte concentrators (p22, paragraphs [0106] and [0107]). Moreover, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a buffer supply system, wherein each separation passage is in fluid communication with separate buffer vials, as taught by Yeung et al. in the electrophoretic apparatus of U.S. Patent No. 6,406,604 in order to supply appropriate buffer to each separation passage of the electrophoretic apparatus to perform CE assays.

Claims 355, 360, 370-373, and 382 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998), and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54).

U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. fails to teach an electrophoresis apparatus, wherein the buffer supply of the first separation passage includes a separation buffer to release the bound first analyte of interest from the immobilized affinity ligands of the first analyte concentrator and the analyte concentrator includes a matrix assembly, which includes a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to further include elution buffer and separation buffer of Heegaard et al. in the buffer supply system of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. in order to perform affinity based CE separations. The advantage of having necessary buffers to conduct affinity-base CE separation, which allows concentration of target analytes prior to CE separation for increased sensitivity, provides the motivation to combine the teachings of Heegaard et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the apparatus of Frankel et al. is designed for affinity-based CE separation. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute beaded microstructure of the analyte concentrator of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a fixed architecture that is fabricated from polymeric microstructures interconnected to each other and to the passage overlapping portion as taught by Heegaard et al. as both configurations, beaded microstructure and a fixed architecture that is fabricated from polymeric microstructures, are art-recognized equivalents in the pre-concentrator applications, where it is immaterial whether the beaded microstructure or the fixed architecture that is fabricated from polymeric microstructures is used.

Claims 362, 364, 365, and 374-376 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997).

U.S. Patent No. 6,406,604 teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 fails to teach an electrophoresis apparatus, further comprising an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means for controlling fluid flow out of auxiliary passage.

Frankel et al. teaches an electrophoresis apparatus as discussed above. Specifically, Frankel et al. teaches an auxiliary passage (1325 in Fig. 13) coupled to at least one of the separation passages downstream of the analyte concentrator to provide a fluid to the separation passage away from the analyte concentrator and valve means (1312 in Fig. 13) for controlling flow out of the auxiliary passage (column 20, lines 21-35).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means as taught by Frankel et al. in the electrophoretic apparatus of U.S. Patent No. 6,406,604 in order to manipulate fluid

movement from the analyte concentrator down the separation passage to the detector system for CE analysis of eluted analytes.

Claim 368 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001).

U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, wherein each of the analyte concentrators has an acoustic micromixing system to improve the reaction in the analyte concentrators.

Yamanishi et al. teaches a filtration chamber comprising acoustic elements as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with acoustic micromixing system of Yamanishi et al. in order to promote, enhance, or facilitate processing or desired biochemical reactions of a sample by mixing of the components within the analyte concentrators of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. The advantage of promoting,

enhancing or facilitating desired biochemical reactions of a sample by mixing of the components within the analyte concentrators provides the motivation to combine the teachings of Yamanishi et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the acoustic micromixing system of Yamanishi et al. is used to cause mixing in biochemical reactions.

Claim 369 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999).

U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, where each of the analyte concentrators has a microwave pulse system to improve the reaction in the analyte concentrators.

Barenburg et al. teaches a microwave radiation device as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a microwave pulse system for applying microwave radiation to a cavity within a microfluidic device as taught by Barenburg et al. in order to

enhance or sometimes make possible the desired result of chemical reactions and processes (improve the reaction in the analyte concentrators). The advantage of enhancing or make possible the desired result of chemical reactions and processes within the analyte concentrators provides the motivation to combine the teachings of Barenburg et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as Barenburg et al. teaches that a microwave pulse system can be used to enhance or sometimes make possible the desired result of chemical reactions.

Claim 377 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,406,604 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) and Yeung et al. (U.S. Patent No. 5,582,705, Dec. 10, 1996) as applied to claim 354 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54) and Fuchs et al. (U.S. Patent No. 5,246,577, Filed May 29, 1990).

U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. teaches an electrophoresis apparatus as discussed above. However, U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. fails to teach an electrophoretic apparatus, wherein the concentration area is surrounded by bulging members to retain the matrix containing immobilized affinity ligands within the concentration area.

Heegaard et al. teaches an on-line solid-phase extraction or preconcentration chambers for affinity capillary electrophoresis as discussed above.

Fuchs et al. teaches an apparatus for concentrating a solute sample as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a matrix assembly having a surface to which the immobilized affinity ligand is bound in the analyte concentrator of U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. as taught by Heegaard et al. in order to use an enrichment chamber design, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability. The advantage of having an analyte concentrator, which permits a larger surface area capacity, enabling a 200- to 5000-fold increase in analyte detectability provides the motivation to combine the teachings of Heegaard et al. and U.S. Patent No. 6,406,604 in view of Robotti et al. and Yeung et al. with a reasonable expectation of success as the analyte concentrator of Heegaard et al. is designed to be used in applications such as CE. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ inlet and outlet of the overlapping portion surrounded by bulging members as taught by Fuchs et al. in the analyte concentrator of Heegaard et al. in order to confine (retain) the matrix containing immobilized affinity ligands (column 1, lines 21-25) within the concentration area since both configurations, the overlapping portion surrounded by bulging members or frits, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the overlapping portion surrounded by bulging members or frits is used to retain the matrix assembly within the overlapping portion of the analyte concentrator. Furthermore, current specification supports that

different embodiments for analyte concentrators with or without frit (p25, paragraph [0112]) are art-recognized equivalents as the originally filed disclosure includes several embodiments, which include the analyte concentrators with frit or bulging members surrounding the overlapping portion. Both embodiments can function to retain matrix assembly in the overlapping portion of the analyte concentrators (p22, paragraphs [0106] and [0107]).

45. Copending Application No. 10/821,328

Claims 322-328, 331, 334, 335, 339-350, 352-361, 364, 366, 367, 371-381, 383-392, 395, 397, 398, 402-411, 413-420, 423, and 425-429 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-77 of copending Application No. 10/821,328 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998).

Copending application teaches an electrophoresis apparatus comprising a transport capillary capable of directing flow of a sample solution to be analyzed, a plurality of separation capillaries coupled to the transport capillary forming a plurality of analyte concentrators having affinity ligands capable of attracting at least one analyte of interest from the sample solution that passes through each of the analyte concentrators. However, copending application fails to specifically teach a plurality of valves located on the transport capillary and on the plurality of separation capillaries, where the valves on the transport capillary control the flow of the sample solution through the transport capillary and the valves on the plurality of separation capillaries control the flow of fluid

through each of the plurality of separation capillaries, whereby each of the analyte concentrators can be localized by the valves on the transport and the plurality of separation capillaries the transport passage entering the separation passage at a side entry location of the analyte concentrator and exiting the separation passage at a side exit location spaced a distance along a length of the separation passage and thereby offset a distance from the separation portion at the entry location, the overlapping portion extending between the entry location and the exit location to form a staggered configuration.

Robotti et al. teaches a microfluidic device comprising two intersecting micro-channels (32 and 34 in Fig.'s 4 and 5) having entry and exit ports and microvalves (36, 38, 39, and 40, positioned along the micro-channels, which localizes the overlapping portion of two intersecting micro-channels, 32 and 34 (Fig.'s 4 and 5 and column 10, lines 13-22). The variation in the placement of micro-channel 34 includes a staggered configuration, wherein the overlapping region of two micro-channels is increased/elongated (Fig. 5). The device of Robotti et al. can be used in a variety of different fluid flow processes such as electrophoretic or chromatographic application (column 10, lines 41-57).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include microvalves positioned along both intersecting transport passage and separation passages as taught by Robotti et al. in the electrophoretic apparatus of the copending Application in order to manipulate fluid flow in applications such as electrophoretic or chromatographic assays, which requires fluid flow control.

The advantage of manipulating fluid flow in the transport passage provides the motivation to combine the teachings of Robotti et al. and the copending Application with reasonable expectation of success as Robotti et al. teaches that the microvalves positioned along two intersecting channels can be used in applications such as electrophoretic or chromatographic assays. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the overlapping portion (analyte concentrator) of the transport and separation passages of the copending Application with the overlapping portion, wherein the overlapping portion extends between the entry location and the exit location of the separation passages to form a staggered configuration as taught by Robotti et al. as both configurations, staggered and non-staggered, are art-recognized equivalents in the microfluidic art applications, where it is immaterial whether the staggered or non-staggered configuration is used. Furthermore, current specification supports that staggered and non-staggered configurations of the transport passage with respect to the separation passage are art-recognized equivalents in the microfluidic art applications as the originally filed disclosure includes two embodiments of the transport passage and separation passages in staggered and non-staggered configuration, which can function to concentrate an analyte in the analyte concentrators (p22, paragraphs [0106] and [0107]).

Claims 329, 330, 332, 333, 362, 363, 365, 393, 394, 396, 421, 422, and 424 are provisionally rejected under the judicially created doctrine of obviousness-type double

patenting as being unpatentable over claims 36-77 of copending Application No. 10/821,328 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322, 354, 385, and 415 above, and further in view of Frankel et al. (U.S. Patent No. 5,637,458, June 10, 1997).

The copending Application in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, the copending Application in view of Robotti et al. fails to teach an electrophoresis apparatus, further comprising an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means for controlling fluid flow out of auxiliary passage.

Frankel et al. teaches an electrophoresis apparatus as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include an auxiliary passage coupled to the separation passage away from the analyte concentrator and valve means as taught by Frankel et al. in the electrophoretic apparatus of the copending Application in view of Robotti et al. in order to manipulate fluid movement from the analyte concentrator down the separation passage to the detector system for CE analysis of eluted analytes.

Claims 336, 368, and 399 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-77 of copending Application No. 10/821,328 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322, 354, and 385 above, and

further in view of Yamanishi et al. (U.S. PG Pub. No. US 2003/0134416 A1, Filed Oct. 11, 2001).

The copending Application in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, the copending Application in view of Robotti et al. fails to teach an electrophoretic apparatus, wherein each of the analyte concentrators has an acoustic micromixing system to improve the reaction in the analyte concentrators.

Yamanishi et al. teaches a filtration chamber comprising acoustic elements as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of the copending Application in view of Robotti et al. with the acoustic micromixing system of Yamanishi et al. in order to promote, enhance, or facilitate processing or desired biochemical reactions of a sample by mixing of the components within the analyte concentrators of the copending Application in view of Robotti et al. The advantage of promoting, enhancing or facilitating desired biochemical reactions of a sample by mixing of the components within the analyte concentrators provides the motivation to combine the teachings of Yamanishi et al. and the copending Application in view of Robotti et al. with a reasonable expectation of success as the acoustic micromixing system of Yamanishi et al. is used to cause mixing in biochemical reactions.

Claims 337, 369, and 400 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-77 of copending Application No. 10/821,328 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322, 354, and 385 above, and further in view of Barenburg et al. (U.S. PG Pub. No. US 2002/0115201 A1, Filed Sept. 16, 1999).

The copending Application in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, the copending Application in view of Robotti et al. fails to teach an electrophoretic apparatus, where each of the analyte concentrators has a microwave pulse system to improve the reaction in the analyte concentrators.

Barenburg et al. teaches a microwave radiation device as discussed above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the apparatus of the copending Application in view of Robotti et al. with a microwave pulse system for applying microwave radiation to a cavity within a microfluidic device as taught by Barenburg et al. in order to enhance or sometimes make possible the desired result of chemical reactions and processes (improve the reaction in the analyte concentrators). The advantage of enhancing or make possible the desired result of chemical reactions and processes within the analyte concentrators provides the motivation to combine the teachings of Barenburg et al. and the copending Application in view of Robotti et al. with a reasonable expectation of

success as Barenburg et al. teaches that a microwave pulse system can be used to enhance or sometimes make possible the desired result of chemical reactions.

Claims 338, 351, 370, 382, 401, and 412 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-77 of copending Application No. 10/821,328 in view of Robotti et al. (U.S. Patent No. 6,375,901, Filed June 29, 1998) as applied to claims 322, 354, and 385 above, and further in view of Heegaard et al. (*Journal of Chromatography B*, Sept. 11, 1998, Vol. 715, pp29-54).

The copending Application in view of Robotti et al. teaches an electrophoresis apparatus as discussed above. However, the copending Application in view of Robotti et al. fails to teach an electrophoretic apparatus, wherein the affinity ligand is covalently bound to a matrix assembly of the analyte concentrator.

Heegaard et al. teaches that affinity compound (affinity ligand) can be attached covalently to an insoluble and porous solid support, which is suitable for chromatography, and utilized to purify a corresponding affinity ligand (analyte, p47, right column, first paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use immobilization method of Heegaard et al., in which an affinity ligand is covalently bound to a matrix assembly of the analyte concentrator of the copending Application in view of Robotti et al. in order to generate a matrix assembly of

the analyte concentrator suitable for chromatography to purify a corresponding analyte prior to CE analysis.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

46. Applicant's arguments with respect to claims 1-39 have been considered but are moot in view of the new ground(s) of rejection.

47. Applicant did not address the objections of the drawings in the Office Action filed on October 28, 2005. Therefore, the objections of the drawings have been maintained.

Conclusion

48. No claim is allowed.

49. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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